NTP
National Toxicology Program

Report to the NTP Board of Scientific Counselors

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Topics

- Actions and priorities
- Recent invited talks
- Ideas and concepts for moving our environmental health mission forward
- NIEHS ARRA opportunities

Actions and Priorities

- Top leadership positions – will be open to national searches
  - Gwen W. Collman, Ph.D., Interim Director, Division of Extramural Research and Training
  - Steven R. Kleeberger, Ph.D., selected to be Acting Deputy Director
  - John B. Pritchard, Ph.D., named Acting Scientific Director
  - Daryl C. Zeldin, M.D., Acting Clinical Director
- Hiring leadership positions in ethics and diversity/education
- Facility sharing with EPA
- Commitment to strengthening relations with NIH, extramural community, and NTP-agency partners
  - New positions at NIH in Bethesda, MD

Recent Invited Talks

- "A New Vision for NIEHS and NTP" - Toxicology Forum, Aspen, CO, July 12-16, 2009
- "Opportunities to Strengthen Environmental Health Research" - IOM Roundtable, Woods Hole, MA, June 29-30, 2009
- "Science, Environment and Public Health: Bringing It Together" - National Conversation on Public Health and Chemical Exposures, Washington, DC, June 26, 2009
- "Green Chemistry and Environmental Health" - Green Chemistry Panel, College Park, MD, June 24, 2009
- "Effects of Brominated Flame Retardants: Health and Regulation" - 11th Annual Workshop on Brominated Flame Retardants, Ottawa, Canada, May 19-20, 2009

"It is our job as scientists to attempt, as best we can, to look into the future, see the changes ahead, and anticipate the side effects of these changes. But we know from past experiences that there are few important and useful discoveries that do not have some unanticipated, undesirable side effects. It is our responsibility to alert leaders in public policy and suggest to them how we might prevent or minimize any negative health consequences."

Dr. David Rall (1990)

NTP
National Toxicology Program

National Institute of Environmental Health Sciences

- Unique institute
- Wide variety of programs supporting our mission of environmental health
  - Intramural laboratories
  - Extramural funding programs
  - National Toxicology Program

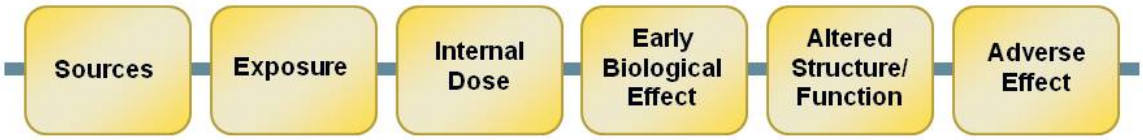
NIEHS and NTP Moving Forward

- Health and Environment is a national priority
- New issues and technologies are emerging
- Assemble the best individual and team science to address complex diseases and complex environmental impacts
- A strong desire to partner with other federal agencies: EPA, CDC, FDA, DOE….
- Improve integration across research disciplines and with all partners
- Improve our translation and communication of basic science findings into human health protection

New and Renewed Emphasis for NTP

- Coordinate toxicity testing across the Federal government
- Develop new methodologies for efficient and thorough toxicological assessments
- Establish dosing during the perinatal period as a default
- Increase understanding of exposure-response relationships and issues of dosimetry
- Develop appropriate safety testing approaches for nanomaterials
- Integrate results from new "data rich" techniques (i.e. genomics, high through-put screening) with traditional toxicology data to provide public health context
- Provide guidance for the proper utilization of new types of information in hazard identification and characterization

Risk Paradigm



What about Timing of Exposure?

- People vary in their susceptibility to the toxic effects of chemical exposures
  - Early life stages
  - Older life stages
  - Pre-existing conditions or genetic-based vulnerabilities
  - People who are more highly exposed

Early Life Exposure and Adult Development of Disease

- Many chronic adult diseases may be traced back to exposures that occurred during development
  - e.g., asthma, diabetes, obesity, heart disease
- *In utero* or neonatal exposures to environmental, dietary, and behavioral changes may make people susceptible to diseases later in life
- Vulnerability of human fetus to outside influences ("Barker Hypothesis")

What Is "Low Dose"?

- The "dose makes the poison" …
  - Different effects occur at different doses
- "Low" dose may just mean "lower" than usually studied
  - The most common definition: below previously identified "adverse" dose level; environmental exposure levels; in the physiological range…

Current NTP Research and Testing Areas

- Cellular phone radiation
- Combination HIV therapies
- Dietary supplements
- DNA-based therapeutics
- Drinking water contaminants
- Endocrine disruptors
- Green chemistry
- Herbal medicines
- Nanoscale materials
- Occupational exposures
- Persistent organic pollutants
- Phototoxicants

Interagency Coordination on Toxicity Testing

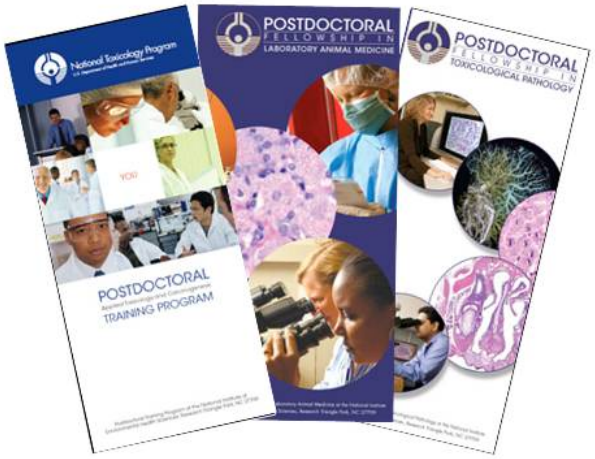
- Nomination of chemical exposures for testing and research
  - FDA priority chemicals
  - ATSDR under the Comprehensive Environmental Response, Compensation, and Liability Act
- Evaluation of nominations and study plans
  - Interagency Committee on Chemical Evaluation and Coordination
  - NTP Executive Committee
- Interagency agreements with FDA/NCTR, CDC/NIOSH, and EPA to carry out testing and research activities
  - Bisphenol A, herbals, dietary supplements, nanoscale materials, mold, phthalates, and phthalate mixtures
  - Characterization of occupational exposures
  - Exposure assessment in occupational settings

Linking Environment, Genes, Pathways, and Diseases

- Identify "disease pathways" and "toxicity pathways"
- Expand strategies for understanding environmental influences on disease and susceptibility
  - Rodent toxicology studies (classical, transgenic, and multi-strain models)
  - High and medium throughput testing (biochemical, cellular, and molecular targets)
  - Lower organism model systems (*C. elegans* and zebrafish)
  - *In vitro* 3-D model systems
  - Computational toxicology
- Use "omics" and molecular tools to validate choices
- Partnering with other federal groups (EPA and NIH Chemical Genomics Center)

NTP Training Programs

- Provide postdoctoral trainees opportunities to build careers
  - Toxicology and carcinogenesis trainees participate as NTP study scientists
  - Pathology trainees gain expertise in diagnostic pathology
  - Laboratory animal medicine trainees gain experience in laboratory animal veterinary care



NIEHS Division of Intramural (DIR)

- Conduct basic, applied, and epidemiological research to understand biological consequences of environmental exposures
  - Interactive and interdisciplinary
  - High risk and long-term research
- 12 laboratories and branches
- New Clinical Research Unit opening July 2009
  - No invasive procedures/inhalation exposures
  - Outside advisory panel

NIEHS Division of Extramural Research and Training (DERT)
A Collaborative Scientific Enterprise

- Children's Environmental Health and Disease Prevention Research Centers
- Centers for Oceans and Human Health
- Obesity and the Built Environment program
- Autism: Early Autism Risk Longitudinal Investigation
- Many more…

NIEHS American Recovery and Reinvestment Act (ARRA) Opportunities

- Total for NIEHS: $187M
  - NIEHS ($168M) plus Superfund ($19M)
- NIEHS signed onto 33 Challenge topics under NIH Challenge Grants
  - 11 topics are high priority for NIEHS
- NIEHS funding priorities for Grand Opportunities grants:
  - Environmental health and safety of engineered nanomaterials
  - Impacts of bisphenol A exposure on human health
- Competitive and administrative supplements
- Small number of R&D contracts
- <$1M for the Intramural Program

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Our Commitment: Understand and Prevent Environmental Influences on Disease